Stupor

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C_2H_5OH

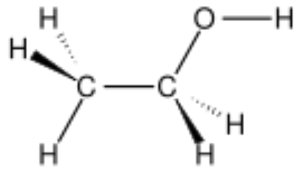

Figure 1 The chemical structure of inhibition.

Ethanol has been the drug of choice for millennia, as it bestows upon the user a feeling of bliss and inhibition. Through the years it has enjoyed the company of prince and pauper alike, reigning its control and aid to various social interactions the world over. To some it has incited envy, rage, and madness and to others, it has given way to new friendships, and lasting ties. In writing assignment two, we will inspect its influence on humanity, and the chemical mechanism as to how this molecule has sculpted societies.

One can only guess what it must've been like for the first homo sapiens to happen upon the effects of ethanol. Truly, great respect must be given to the many who died of experimentation until finally, like a genetic modification providing survival, the first few humans consumed and circulated the drink of choice to withstand the test of time. Though the exact date is not known, there's reason to believe that we began consuming alcohol as early as 10,000 BC.[1] For perspective, the wheel was invented some time around 3,500 BC, and the earliest evidence of writing carbon-dates to about 6000 BC. This means the beverage must have accompanied numerous triumphs in human ingenuity before we could even write about them! By 7000 BC the ancients whom resided in the neolithic village of Jiahu were concocting fermented beverages of rice beer and honey mead.[2] The Babylonians along with Egyptians were known to be drinking by 3000 BC.[3] The Egyptian funerary pictured above depicts bakers working alongside beer brewers. Indeed, Pharaohs were drinking beer made from barely bread while overseeing the construction of pyramids. [4]

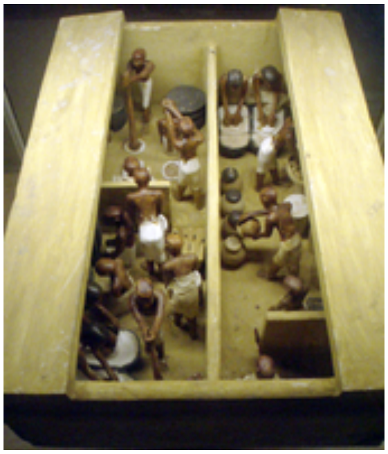

Figure 2: Circa 2009 – 1998 BC[3]

Figure 3: "Bacchus" by Michelangelo (1497)

As ethanol shared an intimate relationship with the progress of human civilization, so too did it find a place in human spirituality. Hinduism speaks of the woes and medicinal benefits of alcohol in its so-called ayurvedic text, while the Greeks came to worship Dionysus, the god of winemaking. A God of many names, he was also known as Bacchus and Elutherios or, "the liberator", which denotes alcohols effects of inhibition. Judaism also speaks of its beneficial effects in the Hebrew Bible (Proverbs 31:6-7):

"Give strong drink unto him that is ready to perish, and wine unto those that be of heavy hearts. Let him drink, and forget his poverty, and remember his misery no more."

But of course, not all religions celebrate its effects. Along with Islam, Buddhism forbids the use of alcohol, and although the ayurvedic Sanskrit text speaks of its use, it advises against its overconsumption. Considering the side effects of heavy drinking it isn't a wonder that some cultures and religions opted to abstain, nevertheless even philosophers found value in the simple molecule.

Democritus of Greece was born in 460 BC, and was known to be a jovial sort, as he was dubbed "the laughing philosopher". A man who once said "A life without parties would be like an endless road without an inn", he enjoyed his drink, and enjoyed the curiosities of life[5]. Because of his contribution to atomic theory and etiology, some even consider him to be the "Father of modern science". No doubt Democritus would've been intrigued to learn the mechanism behind the wine he so loved, and now thanks to those curious like him, we understand more about ethanol than ever before.

The International Union of Pure and Applied Chemistry's systematic name for the drug is indicative of it's two carbons, and single hydroxyl group. Compared to other psychoactive drugs it is incredibly simple in size and shape; its molecular weight is a mere 46.07 g mol^{-1} while that of another widely used substance, THC, is 314.47 g mol^{-1}. Earthly inhabitants can happen upon ethanol by finding fermenting yeast or, one may find ethanol due to the anaerobic germination of plants. For those who find themselves thirsty during interstellar travel, they may decide to bring some yeast with them, or perhaps visit interstellar clouds where ethanol has been detected to form icy coatings around.[6] Because most ethanol consumed today for pleasure has been the byproduct of yeast metabolism, it makes sense to spend some time on this biochemical mechanism, for without it there would be a severe absence of rad parties.

Figure 4: Fermenting grapes[7]

Like us, our distant eukaryotic cousins known as yeast consume sugar for energy. Unlike us, yeast can also do this while deprived of oxygen. Some yeast will take glucose up and convert it directly to carbon dioxide and water. The former of which is why bakers yeast is used to raise bread. However, most strains of yeast such as *Saccharomyces cerevisiae* will produce ethanol no matter the aerobic conditions. In species such as these glucose, exothermically separates into two pyruvate molecules, supplying ATP and NADH in the process. These pyruvate molecules are then converted into acetaldehyde, which results in the production of carbon dioxide. Finally, the acetaldehyde reacts with NADH, yielding the coveted ethanol. The chemical then accumulates in whatever medium the yeast may reside such as grapes in the case of wine, or hops in the case of beer. Industrialized processes have taken advantage of these biochemical reactions for centuries, and all those of age can easily stroll to their local store to purchase the byproduct of these reactions in a form of their choosing. Once the exchange of monetary note for goods has been made, and the deal sealed, the imbibing organism will have their mouth come in contact with the first drops of alcohol, and at that moment begins ethanol's foray into a eukaryotic being far more complex than from whence it came.

Even though the molecule is small, the Danish urban legend of getting drunk by soaking your feet in an alcoholic beverage has proven to be false.[8] The molecule must make its way to the blood stream, which is generally reached orally, though some brave (foolish) folk have consumed it anally, intravenously, nasally, and ocularly. Whichever way one may fancy the addition of ethanol into their person, it diffuses easily through every cell in the body thanks to its high permeability to cellular membranes. In terms of oral consumption, the alcohol will first find its way into the stomach, and then to the small intestine where most of it will be shuttled into the blood stream via the small intestinal walls. From here it reaches the brain, and this is where the action occurs of course. Ethanol is classified as a neurotoxic[9] and psychoactive drug because it affects various neuronal receptors. These include $GABA_A$, and NMDA receptors among others[12]. Interestingly the $GABA_A$ receptor contains sites that can be modified by a host of drugs including benzodiazepines, barbiturates, and inhaled anesthetics[10]. Like many psychoactive drugs the exact molecular mechanism to their psychological manipulation is not yet well understood, but modulation of receptors by novel drugs has proven to give some insight. CL-218,872 is one such drug that targets a subunit of $GABA_A$, and has shown to cause sedative and hypnotic effects, as well amnestic action[11] (a property of alcohol that has long been the crux of regretful actions). Similarly the NMDA rece-

-ptors have been implicated in anesthesia and even hallucinations, though ethanol is only a weak modulator of this receptor. As said, the exact mechanisms behind what brings about euphoria and inhibition are complex, and involve the interaction of many receptors in the brain, therefore it must be emphasized that the two receptors mentioned here are only a small insight into its true neurological affect.

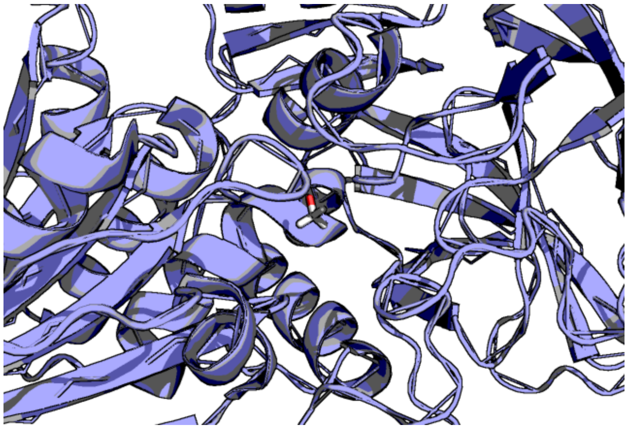
Figure 6: Active site of Alcohol Dehydrogenase

While some ethanol molecules toil away at modulating receptors in the brain, they are continually reaching their ultimate demise in the liver, at an average rate of about 0.5 oz per hour. Within the liver are cells with a large amount of smooth endoplasmic reticulum where detoxification occurs primarily through the enzyme alcohol dehydrogenase (it should be noted this enzyme has many roles outside alcohol detoxification). The enzyme, along with zinc yields acetaldehyde by use of NAD, which is further metabolized by acetaldehyde dehydrogenase. Outside of the liver, cytochrome P450 metabolizes ethanol, similarly yielding acetaldehyde. When it’s all said and done, the organism successfully rids itself of the poison, and confronts reality with stark sobriety. Cheers to those who end each intoxication with refreshing vitality rather than harrowing regret!

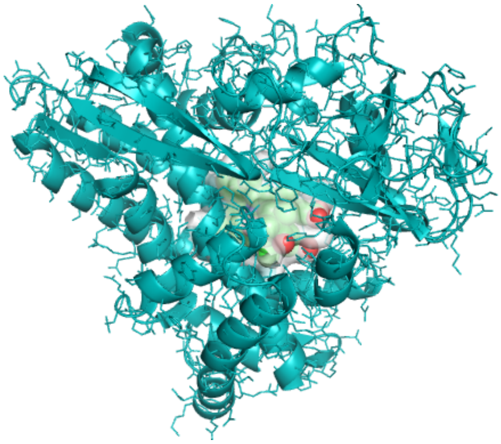
Figure 5: Active site of Cytochrome P450

References

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